

**UNITED STATES DISTRICT COURT  
DISTRICT OF DELAWARE**

PACIFIC BIOSCIENCES OF CALIFORNIA, INC.,

*Plaintiff,*

vs.

OXFORD NANOPORE TECHNOLOGIES, INC.  
and OXFORD NANOPORE TECHNOLOGIES,  
LTD.

*Defendant.*

C. A. No. 17-cv-275-LPS

JURY TRIAL DEMANDED

**FIRST AMENDED COMPLAINT FOR PATENT INFRINGEMENT**

Plaintiff Pacific Biosciences of California, Inc. (“Plaintiff” or “PacBio”) for its First Amended Complaint against Defendants Oxford Nanopore Technologies, Inc. (“ONT, Inc.”) and Oxford Nanopore Technologies, Ltd. (“ONT, Ltd.”) (“collectively Defendants”) alleges and states the following:

**NATURE OF THE ACTION**

1. This is an action for patent infringement arising under the United States Patent Act, 35 U.S.C. §§1, *et seq.*, including 35 U.S.C. § 271.

2. PacBio brings this action to halt Defendants’ infringement of PacBio’s rights under the Patent Laws of the United States 35 U.S.C. § 1, *et seq.*, which arise under U.S. Patent No. 9,546,400 (“the ’400 patent”).

**THE PARTIES**

3. PacBio is a corporation organized and existing under the laws of the State of Delaware, having a principal place of business at 1305 O’Brien Drive, Menlo Park, California 94025.

4. PacBio was founded in the year 2000 and develops, manufactures, and sells a novel DNA sequencing platform that helps researchers resolve genetically complex problems. PacBio's DNA sequencing technology is based on real-time detection of the incorporation of nucleotides into a single strand of DNA. That technology goes by the name "SMRT®" sequencing, which is short for "Single Molecule, Real-Time" sequencing. PacBio's SMRT® sequencing platform encompasses not just DNA sequencing instruments, but also novel sequencing chips and chemical reagents for use with PacBio's DNA sequencing instrument and sophisticated software for analyzing the data that emerges from PacBio's sequencing instruments.

5. PacBio's SMRT® Sequencing Platform and technology allows researchers to carry out numerous applications, including at least (1) de novo genome assembly to finish genomes in order to more fully identify, annotate, and decipher genomic structures; (2) targeted sequencing to more comprehensively characterize genetic variations; and (3) identification of DNA base modifications to help characterize epigenetic regulation and DNA damage. PacBio's SMRT® Sequencing Platform and technology provides high accuracy, ultra-long reads, uniform coverage, and is believed to be the only DNA sequencing technology that provides the ability to simultaneously detect epigenetic changes.

6. In addition to the commercialization of its flagship SMRT® sequencing platform, PacBio has broad expertise in single-molecule sequencing and is engaged in exploratory work related to single-molecule sequencing, including techniques related to single-molecule sequencing based on detection platforms such as nanopores. Collectively, PacBio's research and development efforts have resulted in a patent portfolio that includes over 330 issued U.S. patents and pending applications related to single-molecule sequencing techniques.

7. Defendant ONT, Inc. is a corporation organized under the laws of Delaware with its principal place of business at 1 Kendall Square, Bldg. 200, Cambridge, Massachusetts 02139. On information and belief, ONT, Inc. is engaged in the commercialization throughout the United States of nanopore-based single-molecule sequencing products, including at least the MinION, GridION X5, PromethION, SmidgION, and Flongle sequencing instruments, reagents and kits for use with these instruments, and the 2D and 1D Squared products.

8. Defendant ONT, Ltd. is the corporate parent of ONT, Inc. and is a corporation organized under the laws of England and Wales with its principal place of business at Edmund Cartwright House, 4 Robert Robinson Avenue, Oxford Science Park, Oxford, OX4 4GA, UK. On information and belief, ONT, Ltd. is engaged in the design, manufacture, importation into the United States, sale for importation, and commercialization throughout the United States of nanopore-based single-molecule sequencing products, including at least the MinION, GridION X5, PromethION, SmidgION, and Flongle sequencing instruments, reagents and kits for use with these instruments, and the 2D and 1D Squared products.

### **JURISDICTION AND VENUE**

9. This action arises under the Patent Laws of the United States, Title 35, United States Code, §§ 1 *et seq.*, including 35 U.S.C. §§ 271 and 281.

10. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. §§ 1331 and 1338(a).

11. This Court has personal jurisdiction over defendant ONT, Inc. ONT, Inc. has substantial contacts with the forum as a consequence of conducting business in Delaware, and has purposefully availed itself of the benefits and protections of Delaware state law by incorporating under Delaware law.

12. This Court also has personal jurisdiction over ONT, Ltd. ONT, Ltd. has purposefully availed itself of the benefits of Delaware's laws and of the privilege of conducting business in Delaware by directing into Delaware products that embody the patents-in-suit. ONT, Ltd. for instance has broadly targeted the United States as a market for its products and, as part of these efforts, has specifically targeted the Delaware market, including Delaware organizations and companies such as the University of Delaware, DuPont, and AstraZeneca. Upon information and belief, in addition to making its products available for purchase in Delaware through its website, ONT, Ltd. and its staff have specifically identified Delaware organizations as potential customers for its products and have successfully reached out to these customers and placed their products with these customers and subsequently provided particularized support services and received feedback.

13. For instance, upon information and belief, ONT, Ltd. has provided genetics laboratories at the University of Delaware with its sequencing products. One laboratory at the University of Delaware claims to have as a member a "resident expert" on Defendants' MinION sequencing platform. *See* Exhibit 13. Upon information and belief, in connection with the provision of its sequencing products to the University of Delaware, ONT, Ltd. has contracted with the University of Delaware and/or Delaware residents affiliated with the University of Delaware to impose terms and conditions upon their receipt and use of Defendants' sequencing equipment. Attached hereto as Exhibits 14 and 15 are exemplary agreements governing the relationship between ONT, Ltd. and its Delaware customers. Among other things, these agreements impose restrictions on how Defendants' equipment may be used, grants license rights, imposes confidentiality duties, grants audit rights, provides for supports services, and limits publication rights. These agreements are expressly between Defendants' customers and

ONT, Ltd. and thus show that ONT, Ltd. has actively engaged in business in this district and taken an active role in governing its relationship with its Delaware customers.

14. Additionally, upon information and belief, ONT, Ltd.'s highest-ranking business development corporate officers have specifically contacted individuals at Delaware organizations and entities (such as the University of Delaware and DuPont) to inter alia enter into research collaborations, provide product status updates, receive product feedback, provide technical support, share research results, and arrange for in-person meetings. On the foregoing bases, ONT, Ltd. has had substantial contacts with this jurisdiction sufficient to subject it to jurisdiction in this district.

15. At a minimum, this Court has jurisdiction over ONT, Ltd. because ONT, Inc. and ONT, Ltd. are alter egos and/or agents of each other in connection with performance of the infringing acts below. Upon information and belief, the following facts, in addition to those contained in the rest of this complaint, demonstrate that ONT, Inc. and ONT, Ltd. share a unified governance, interest, and ownership in connection with the infringing acts identified below such that to the extent the Court exercises jurisdiction over ONT, Inc., it may also exercise jurisdiction over ONT, Ltd.

16. Upon information and belief, ONT, Ltd. and ONT, Inc. share overlapping officers and there is no meaningful distinction in the governance of the two entities. For instance, in addition to acting as both the President and a Director of ONT, Inc., Spike Willcocks serves as the Chief Business Development Office of ONT, Ltd. Likewise, in addition to acting as Treasurer, Secretary, and Director of ONT, Inc., James McDonald acts the Vice President of Finance for ONT, Ltd. Upon information and belief, the day-to-day activities of ONT, Inc. are

effectively governed by ONT, Ltd. such that there is effectively no distinction between the two corporate entities.

17. Consistent with the foregoing, upon information and belief, the highest-ranking officers of ONT, Inc. either self-identify on social media as officers of ONT, Ltd. or make no distinction between the two different ONT companies, confirming that ONT, Inc. and ONT, Ltd. are effectively alter egos. Attached as Exhibits 16, 17, and 18 are the LinkedIn profiles of the official officers of ONT, Inc. (Sissel Juul, Spike Willcocks, and James Brayer) showing that none identify themselves as employees of ONT, Inc.

18. As yet further confirmation that there is effectively no distinction between ONT, Inc. and ONT, Ltd., there is no distinct website for ONT, Inc. All of Defendants' United States locations—including any locations ostensibly affiliated with ONT, Inc.—are portrayed on Defendants' website as being part of a single unified entity under the umbrella of the primary ONT, Ltd. location in England. Consistent with this, Defendants' website offers a single unified contact point for inter alia purchase inquiries, support inquiries, employment inquiries, product information, and company news updates. Attached as Exhibit 19 is an excerpt from Defendants' website showing how their different locations are portrayed in a unified manner.

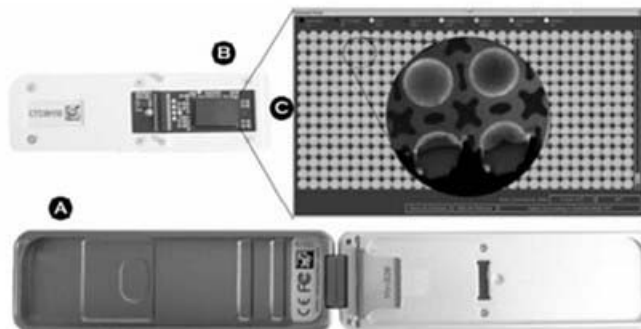
19. As yet another example, upon information and belief, ONT, Inc. and ONT, Ltd. share the same internal and external legal counsel. In connection with both this litigation and ongoing ITC litigation involving ONT, Ltd., Defendants' are represented by outside counsel at Baker Botts LLP. Likewise, upon information and belief, this litigation has been managed not by a dedicated ONT, Inc. employee, but by James McDonald, ONT, Ltd.'s Vice President of Finance.

20. Venue is proper in this District under 28 U.S.C. §§ 1391(b) and (c), and 1400(b) because (1) ONT, Inc. is a Delaware corporation, (2) ONT, Ltd. is an alien corporation subject to venue in any district and (3) Delaware is a convenient forum for resolution of the parties' disputes set forth herein.

### **BACKGROUND**

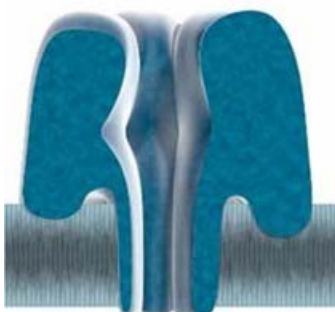
21. On information and belief, in the 2015 timeframe Defendants began commercializing single-molecule sequencing products based on the use of protein nanopores. Defendants purport to offer single-molecule sequencing products that, like PacBio's products, are capable of determining the sequence of long stretches of DNA in a single pass. The ability to generate such "long reads" is an area where PacBio has and continues to be widely recognized as the technical and commercial leader. PacBio and Defendants compete in the single-molecule sequencing market.

22. Defendants' single-molecule sequencing products include at least the MinION, GridION X5, PromethION, SmidgION, and Flongle sequencing systems and reagents, consumables, and software for use with same, including without limitation reagents and kits used to generate "2D reads" and "1D squared reads" using Defendants' sequencing instruments (collectively, the "Accused Products"). For example, two views of a representative MinION device are shown below:



**Figure 4.** (A) MinION Mk1 (B) flow cell (C) nanopore array (Individual nanopore cells reproduced, modified, with permission from Oxford Nanopore).

Exhibit 3; Exhibit 4 at 292. The top image shows a working MinION device, and the bottom view shows the interior of the device. The portion labeled “C” in the above photograph depicts a flow cell with an array of individual nanopores. Nanopores are tiny holes embedded into a membrane and are formed by inserting proteins that have a hollow tube through their center into a polymer membrane, as shown in the image below:



See Exhibit 5. The Accused Products each include one or more flow cells that include a “nanopore array.”



23. While the MinION instrument includes a single flow cell, the PromethION instrument includes 48 flow cells and has been described as a “whole box of MinION sequencers.” Exhibit 6. A representative PromethION instrument with its 48 flow cells is shown below:



*Id.*

24. To sequence DNA using Defendants’ products, one first applies a voltage across the membrane such that an electrical current flows through the hole. A strand of DNA is then drawn through the hole:



Exhibit 7. As the DNA passes through the hole, it disrupts the electrical current that is passing through the hole, thus producing a signal. To evaluate the sequence, one can attempt to correlate this signal with the DNA bases that are passing through the hole.

25. More particularly, in nanopore-based DNA sequencing systems, such as those sold by Defendants, the signal that results from passage of the DNA through the nanopore arises not just from a single DNA base, but from a contiguous group of DNA bases that interacts with the nanopore at a given time. Therefore, to determine the DNA sequence, Defendants' nanopore uses calibration information produced by measuring the signals from the different combinations of bases that may interact with the nanopore at a given time.

26. Defendants infringe, literally or under the doctrine of equivalents, PacBio's '400 patent through their activities connected to their nanopore sequencing products. For instance, representative claim 1 of the '400 patent is listed below:

1. A method for sequencing a nucleic acid template comprising:
  - a) providing a substrate comprising a nanopore in contact with a solution, the solution comprising a template nucleic acid above the nanopore;
  - b) providing a voltage across the nanopore;

- c) measuring a property which has a value that varies for N monomeric units of the template nucleic acid in the pore, wherein the measuring is performed as a function of time, while the template nucleic acid is translocating through the nanopore, wherein N is three or greater; and
- d) determining the sequence of the template nucleic acid using the measured property from step (c) by performing a process including comparing the measured property from step (c) to calibration information produced by measuring such property for 4 to the N sequence combinations.

27. Use of Defendants' sequencing products leads to direct infringement of this claim in the following way. First, Defendants' products include nucleic acid sequencing instrument having a nanopore-containing membrane that is in contact with a solution (step a). A voltage is then applied across the membrane to drive a current across the membrane (step b). A nucleic acid molecule to be sequenced is then drawn through the nanopore, and, as a result, the current is disrupted in a time-dependent manner that varies based on the N (wherein N is three or greater) monomeric nucleic acid bases that are interacting with the pore at a given time (step c). An artificial neural network is then used to compare the signal obtained from drawing the nucleic acid through the nanopore to calibration information obtained from measuring such a signal from the 4 to the N combinations of bases, thus allowing one to determine the sequence of the nucleic acid (step d).

28. As an example, attached hereto as Exhibit 2 is a preliminary and exemplary claim chart detailing Defendants' infringement of multiple claims of the '400 patent. This chart is not intended to limit PacBio's right to modify the chart or allege that other activities of Defendants' infringe the identified claims or any other claims of the '400 patent or any other patents. Exhibit 2 is hereby incorporated by reference in its entirety. Each claim element in Exhibit 2 that is mapped to Defendants' product shall be considered an allegation within the meaning of the Federal Rules of Civil Procedure and therefore a response to each allegation is required.

**COUNT I**  
**(Infringement of U.S. Patent No. 9,546,400)**

29. Plaintiff repeats and re-alleges each and every allegation contained in the preceding paragraphs of this Complaint as if stated in their entirety herein, and incorporates them herein by reference.

30. The '400 patent, entitled "Nanopore Sequencing Using N-mers," issued on January 17, 2017, to inventors Steven Turner and Benjamin Flusberg. The '400 patent is assigned on its face to Plaintiff PacBio. PacBio is the owner of all rights, title to and interest in the '400 patent.

31. On information and belief, Defendants' have infringed and continues to infringe at least claims 1-8, 10, and 14-15 of the '400 patent pursuant to 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by using within the United States without authority the Accused Products. As an example, attached as Exhibit 3 is a preliminary and exemplary claim chart detailing Defendants' infringement of these claims of the '400 patent. This chart is not intended to limit PacBio's right to modify the chart or allege that other activities of Defendants infringe the identified claims or any other claims of the '400 patent or any other patents. Exhibit 3 is hereby incorporated by reference in its entirety. Each claim element in Exhibit 2 that is mapped to the Accused Products shall be considered an allegation within the meaning of the Federal Rules of Civil Procedure and therefore a response to each allegation is required.

32. Defendants have had knowledge of and notice of the '400 patent and their infringement long before the filing of this complaint. For instance, on March 21, 2016, Defendants cited PacBio's U.S. Patent Application Publication No. 2010/0331194 in an information disclosure statement during prosecution of Defendants' U.S. Patent Application No. 13/147,159. *See* Ex. 12 at 5. The application that published as PacBio's Publication No.

2010/0331194 is the parent of the application that issued as the '400 patent, and as such shares the same specification as the '400 patent. On information and belief, Defendants have monitored PacBio's patent filings and has been aware of the '400 patent since its issuance on January 17, 2017. At a minimum, Defendants have had knowledge of and notice of the '400 patent and its infringement since at least, and through, the filing and service of PacBio's complaint in this action and despite this knowledge continues to commit the aforementioned infringing acts.

33. Defendants actively, knowingly, and intentionally has induced, or has threatened to induce, infringement of at least claims 1-8, 10, and 14-15 of the '400 patent through a range of activities. First, on information and belief, Defendants have induced infringement by controlling the design and manufacture of, offering for sale, and selling the Accused Products with the knowledge and specific intent that its customers will use these instruments to infringe, literally or under the doctrine of equivalents, by performing the claimed method for sequencing a nucleic acid template. For instance, Defendants have admitted in an ongoing International Trade Commission investigation that it imports, sold for importation, and or/sells its MinION product and PromethION product within the United States. *See* Ex. 8 ¶ 53.

34. Second, on information and belief, Defendants have induced infringement by their customers through the dissemination of promotional and marketing materials relating to the Accused Products with the knowledge and specific intent that their customers will use these instruments to infringe, literally or under the doctrine of equivalents, by performing the claimed method for sequencing a nucleic acid template. For instance, Defendants promote the Accused Products on their website, stating that their products offer numerous benefits such as real-time DNA/RNA sequencing, no capital cost, long reads, scalability, high-fidelity, and rapid library preparation time. *See* Ex. 9.

35. Third, on information and belief, Defendants have induced infringement by their customers through the creation of distribution channels for the Accused Products in the United States with the knowledge and specific intent that their customers will use these instruments to infringe, literally or under the doctrine of equivalents, by performing the claimed method for sequencing a nucleic acid template. For instance, Defendants' website allows customers in the United States to purchase starter packs for Defendants' MinION instruments that, when used, will lead to infringement of the '400 patent. As Defendants' website states, "[b]uy a Starter Pack to join the growing numbers in the Nanopore Community." *See* Ex. 10. As another example, Defendants have created an early access program for its PromethION instrument that provides access to a PromethION device, site installation support, flow cells and reagents, and further information and support. *See* Ex. 11.

36. Fourth, on information and belief, Defendants have induced infringement through the distribution of other instructional materials, product manuals, and technical materials with the knowledge and the specific intent to encourage and facilitate their customer's infringing (either literally or under the doctrine of equivalents) use of the Accused Products. Defendants are liable for their induced infringement of the '400 patent pursuant to 35 U.S.C. § 271 (b).

37. Defendants have contributed to, or has threatened to contribute to, the infringement by their customers of the '400 patent by, without authority, selling and offering to sell within the United States materials and apparatuses for practicing the claimed invention of the '400 patent, including at least the MinION and PromethION instruments. When, for example, either of these instruments is used by Defendants' customers for nucleic acid sequencing, the claimed method of the '400 patent for sequencing a nucleic acid template is performed, thereby

infringing, literally or under the doctrine of equivalents, at least claims 1-8, 10, and 14-15 of the '400 patent.

38. On information and belief, Defendants know that the Accused Products constitute a material part of the inventions of the '400 patent and that they are not a staple article or commodity of commerce suitable for substantial noninfringing use. As documented above, the Accused Products consist of specialized substrates containing protein nanopores that are used in conjunction with specialized reagents for the purpose of sequencing nucleic acid templates. *See supra* ¶¶ 21-28. As such, none of the Accused Products nor any of the reagent kits for use with these instruments is a staple article of commerce suitable for substantial non-infringing use. Defendants know that these instruments are not staple articles or commodities of commerce suitable for substantial non-infringing use because they have no use apart from infringing the '400 patent. Defendants are liable for their contributory infringement of the '400 patent pursuant to 35 U.S.C. § 271(c).

39. Defendants' infringement of the '400 patent has injured PacBio in its business and property rights. PacBio is entitled to recover monetary damages for such injuries pursuant to 35 U.S.C. § 284 in an amount to be determined at trial. Defendants' infringement of the '400 patent has caused irreparable harm to Plaintiffs and will continue to cause such harm unless and until Defendants' infringing activities are enjoined by this Court

#### **PRAYER FOR RELIEF**

WHEREFORE, prays for relief as follows:

- A. Judgment that Defendants have infringed the '400 patent;
- B. An order permanently enjoining Defendants from further infringement of the '400 patent;

C. An award of damages pursuant to 35 U.S.C. § 284 plus pre-judgment and post-judgment interest;

D. An award to PacBio of its costs and reasonable expenses to the fullest extent permitted by law;

E. A declaration that this case is exceptional pursuant to 35 U.S.C. § 285, and an award of attorneys' fees and costs; and

F. An award of such other and further relief as the Court may deem just and proper.

**DEMAND FOR JURY TRIAL**

Pursuant to Federal Rule of Civil Procedure 38(b), PacBio hereby demands a trial by jury on all issues so triable.

Dated: August 23, 2018

Respectfully submitted,

FARNAN LLP

/s/ Brian E. Farnan

Brian E. Farnan (Bar No. 4089)  
Michael J. Farnan (Bar No. 5165)  
919 N. Market St., 12th Floor  
Wilmington, DE 19801  
Telephone: 302-777-0300  
Facsimile: 302-777-0301  
bfarnan@farnanlaw.com  
mfarnan@farnanlaw.com

Edward R. Reines (admitted *pro hac vice*)  
Derek C. Walter (admitted *pro hac vice*)  
WEIL, GOTSHAL & MANGES LLP  
201 Redwood Shores Parkway  
Redwood Shores, CA 94065  
Telephone: 650-802-3000  
Facsimile: 650-802-  
ed.reines@weil.com  
derek.walter@weil.com  
*Attorneys for Plaintiff*